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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,938	12/11/2001	Kenneth Richards	702-011069	4594

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EXAMINER	
MEHTA, ASHWIN D	
ART UNIT	PAPER NUMBER
1638	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,938	RICHARDS ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. Figure 2 contains parts A and B. However, the brief description to Figure 2 on page 10 does not refer to the two parts. The brief description should refer to parts 2A and 2B in the figure. See MPEP 601.01(g). It is suggested that the recitation --(A-B)-- be inserted in line 18 on page 10 after "Figure 2."

Claim Objections

2. Claims 30 and 53 are objected to under 37 CFR 1.75 (b) as being duplicate claims. Both method claims require regenerating a BNYVV resistant sugar beet plant from plant cells comprising the same DNA fragment. Applicant is required to cancel one of the claims, or amend the claim(s).

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 45-52 and 54-57 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are broadly drawn towards a plant cell exhibiting a resistance to beet necrotic yellow vein virus (BNYVV), comprising in its genome a DNA fragment of at least 15

nucleotides in a sequence that that is at least 70% or 80% homologous to the corresponding nucleotide sequence of RNA 1 of said virus; a sugar beet plant exhibiting a resistance to BNYVV consisting at least partly of said cells; progeny, seeds, and structures from said plant.

The claims read on plant cells, plants, and plant parts per se which can be found in nature and thus, are unpatentable. The plants and plant parts, as claimed, have the same utility as those found naturally and therefore do not constitute patentable subject matter. See American Wood v. Fiber Disintegrating Co., 90 U.S. 566 (1974), American Fruit Growers v. Brodgex Co., 283 U.S. 2 (1931), Funk Brothers Seed Co. v. Kalo Inoculant Co., 33 U.S. 127 (1948), Diamond v. Chakrabarty, 206 USPQ 193 (1980). It is suggested that the claims be amended to recite the term "transgenic" in connection with the plant cells, plants, and plant parts to identify products that are not found in nature.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 32-57, 60, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 32-35, 40-43, and 47-50: the recitation "the fragment has a nucleic acid sequence that corresponds with the homology indicated in claim 30 (or 38 or 45)" renders the claims indefinite. It is not exactly clear what is meant by the recitation. The recitation appears to be limiting the region of RNA 1 that the DNA fragment is to share homology with. If this is

Applicants' intention, it is suggested that the recitation be replaced with --the sequence of said fragment has at least 70% homology--.

In claims 32-36, 40-44, 47-51: the claims recite numbers of nucleotide sequences of RNA 1 of BNYVV. However, there are many different isolates of BNYVV, and they do not share exactly the same nucleotide sequences. For example, Saito et al. (Arch. Virol., 1996, Vol. 141, pages 2163-2175) compare the nucleotide sequences of different BNYVV isolates (pages 2165-2173). It is not clear to which nucleotide sequence of the RNA 1 of which BNYVV isolate the claims are referring to.

In claims 37 and 38: the term "harboring" in line 2 of the claims renders them indefinite. The meaning of the term is not exactly clear. It is suggested that it be replaced with --comprising--.

In claims 45 and 54: the recitation "a resistance" in line 1 renders the claim indefinite. The article "a" suggests more than one type of resistance. The specification at page 3, lines 22-26, indicates that in resistant plants there is little or no virus replication. It is not clear what other types of resistance are encompassed by "a" resistance. It is suggested that the article "a" be deleted from the claim.

In claim 52: the recitation "being part of the sugar beet plant that is resistant against BNYVV" renders the claim indefinite. It is not clear if the recitation is indicating that the plant host already has resistance against BNYVV. It is suggested that the recitation be replaced with --wherein said cell is part of a sugar beet plant--.

In claim 54: the recitation "consisting at least partly of" in lines 1-2 renders the claim indefinite. "Consisting" is closed claimed language. It is not clear if the plant comprises, or only

consists, the plant cells of claim 45. It is suggested that the recitation be replaced with --comprising the plant cells--.

In claims 55-57: the claims are indefinite because it is not clear if the claimed progeny, seeds, or structures have resistance against BNYVV, and if they comprise the cells that comprise the DNA fragment.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 30-35, 37-43, 45-50, and 52-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards a method for conveying resistance to BNYVV to a sugar beet plant, comprising preparing a DNA fragment of at least 15 nucleotides in a sequence that is at least 70%, 80%, 90%, or 95% homologous to the corresponding nucleotide sequence of the genomic RNA 1 of the BNYVV, introducing the DNA fragment into a sugar beet plant cell, and regenerating a transgenic sugar beet plant from the transformed cell; a transformation vector harboring said fragment; a plant cell exhibiting a resistance to BNYVV, comprising said fragment; a method for the production of a sugar beet plant resistant to BNYVV comprising regenerating said plant cell; a sugar beet plant comprising said cells.

The specification indicates that nucleotides 153-3258 of RNA 1 of the BNYVV isolate taught by Bouzoubaa et al. (J. Gen. Virol., 1987, Vol. 68, pages 615-626) was inserted into an Agrobacterium binary transformation vector, operably linked to the CaMV 35S promoter in the sense or antisense direction. RNA 1 of BNYVV encodes the viral replicase. Sugar beet plants were transformed with one or the other vector via Agrobacterium. Seeds from the transformants were produced either by self-pollination or cross-pollination on male sterile plants. Bioassays for BNYVV resistance were carried out on seedlings grown from the F1 transgenic seeds. Only one transgenic line, designated "T157-01,"which contains the RNA1 sequence in sense orientation, had plants that showed BNYVV resistance. The primary transformant of the resistant line had 3 T-DNA inserts (pages 11-14, Examples 1-2). Other F1 plants of this line did, however, also contain plants that showed normal viral susceptibility. The resistant and susceptible plants in the F1 T157-01 line were analyzed in a Southern hybridization, in an attempt to discern the differences in the plants. The introduced T-DNA contained the GUS selectable marker gene. The genomes of the plants were digested with SacI and probed with GUS coding sequence. The results showed that all of the virus susceptible, GUS(+) plants had one cross-reacting band on the Southern blot, whereas the resistant, GUS(+) plants had 2 or 3 bands (pages 14-16, Example 3).

However, the specification does not describe any sequences that share 70%, 80%, 90%, or 95% homology with the RNA 1 sequence of the BNYVV isolate used in the examples, or fragments thereof, that also retain the activity of conferring BNYVV resistance. The structural features of nucleotides 153-3258 of RNA 1 that are essential to the conferred viral resistance are not described. Differences in the sequence then cannot be correlated with the virus resistance

function. Other sequences of RNA 1 have not been correlated with the function of conferring viral resistance in sugar beet plants. See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), where it states: "The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA... Accordingly, the specification does not provide a written description of the invention..." Also see Fiers 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims encompassing DNA fragments of at least 15 nucleotides that have at least 70%, 80%, 90%, or 95% homology to a corresponding sequence of RNA 1 of any BNYVV isolate, and lack of guidance as discussed above, the specification fails to provide an adequate written description of the multitude of nucleotide sequences encompassed by the claims.

6. Claims 30-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for conveying BNYVV resistance to transgenic sugar beet plants expressing nucleotides 153-3258 of RNA 1 of the BNYVV isolate taught by Bouzoubaa et al., does not reasonably provide enablement for virus resistance conferred by any 15 nucleotide fragment, other fragments of RNA 1, or nucleotide sequences that are at least 15 nucleotides long and that have at least 70%, 80%, 90%, or 95% homology to the corresponding region of

RNA 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards a method for conveying resistance to BNYVV to a sugar beet plant, comprising preparing a DNA fragment of at least 15 nucleotides in a sequence that is at least 70%, 80%, 90%, or 95% homologous to the corresponding nucleotide sequence of the genomic RNA 1 of the BNYVV, introducing the DNA fragment into a sugar beet plant cell, and regenerating a transgenic sugar beet plant from the transformed cell; a transformation vector harboring said fragment; a plant cell exhibiting a resistance to BNYVV, comprising said fragment; a method for the production of a sugar beet plant resistant to BNYVV comprising regenerating said plant cell; a sugar beet plant comprising said cells.

The specification indicates that nucleotides 153-3258 of RNA 1 of the BNYVV isolate taught by Bouzoubaa et al. (J. Gen. Virol., 1987, Vol. 68, pages 615-626) was inserted into an Agrobacterium binary transformation vector, operably linked to the CaMV 35S promoter in the sense or antisense direction. RNA 1 of BNYVV encodes the viral replicase. Sugar beet plants were transformed with one or the other vector via Agrobacterium. Seeds from the transformants were produced either by self-pollination or cross-pollination on male sterile plants. Bioassays for BNYVV resistance were carried out on seedlings grown from the F1 transgenic seeds. Only one transgenic line, designated "T157-01,"which contains the RNA1 sequence in sense orientation, had plants that showed BNYVV resistance. The primary transformant of the resistant line had 3 T-DNA inserts (pages 11-14, Examples 1-2). Other F1 plants of this line did, however, also contain plants that showed normal viral susceptibility. The resistant and

susceptible plants in the F1 T157-01 line were analyzed in a Southern hybridization, in an attempt to discern the differences in the plants. The introduced T-DNA contained the GUS selectable marker gene. The genomes of the plants were digested with SacI and probed with GUS coding sequence. The results showed that all of the virus susceptible, GUS(+) plants had one cross-reacting band on the Southern blot, whereas the resistant, GUS(+) plants had 2 or 3 bands (pages 14-16, Example 3).

However, the specification does not teach any other fragments of RNA 1 that confers BNYVV resistance when expressed in transgenic sugar beet. The specification does not teach the sequences within the 153-3258 nucleotide fragment of RNA1 that are essential to its viral resistance activity. In the absence of this guidance, undue experimentation would be required by one skilled in the art to determine how this nucleotide fragment can be changed while retaining its virus-resistance activity. No other RNA 1 fragments, and therefore fragments having at least 70%, 80%, 90%, or 95% homology with it, were shown to confer BNYVV resistance. No guidance at all is provided as to which 15 nucleotide fragments can be used in the claimed method, nor is there any reason provided why one should expect any such fragment to confer viral resistance. The RNA 1 strand of BNYVV consists of well over 6000 nucleotides. The RNA1 strand of the BNYVV isolate taught by Bouzoubaa et al., "F2," consists of 6746 nucleotides. Yet, the specification provides no guidance at all as to which 15 nucleotide stretches would confer viral resistance. It would require undue experimentation to determine which 15 nucleotide fragments can be used with the claimed method.

The specification briefly mentions, on page 6, lines 11-12, that sometimes a gene that is introduced into and expressed in plant causes co-suppression. However, no further guidance is

mentioned as to how one would use fragments of RNA 1 to cause co-suppression. Tang et al. (Genes Dev., 2003, Vol. 17, pages 49-63) assert that 21-26 nt RNAs are formed as part of RNA silencing (co-suppression) in plants (page 49). It is then not clear how any 15 nucleotide fragment can be expected to confer resistance in the claimed method. Further, as it is well known that co-suppression is based on homology between the nucleotide sequences, it is unknown what sequences of BNYVV RNA1 would confer resistance to BNVYY when expressed in transgenic plants cells without also suppressing an endogenous gene that shares homology with the transgenic sequence. Furtherstill, Tang et al. teach that in plants, microRNAs (miRNAs) are also formed as part of the co-suppression/post transcriptional gene silencing pathway, and that these miRNAs have high complementarity to their targets (pages 49-50). It is then not clear, in the absence of further guidance, how fragments that can share as little as 70% homology to any fragment of RNA 1 of BNYVV as small as 15 nucleotides can be used in the claimed method to confer viral resistance. Given the breadth of the claims encompassing the conference of BNYVV resistance by nucleotide fragments as small as 15 nucleotides, and which can have at least 70%, 80%, 90%, and 95% homology with the corresponding fragment of RNA1 of BNYVV, unpredictability of the art and lack of guidance of the specification, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 30-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baulcombe (Plant Cell, 1996, Vol. 8, pages 1833-1844) in combination with Saito et al. (Arch. Virol., 1996, Vol. 141, pages 2163-2175), and Hall et al. (Nature Biotech., 1996, Vol. 14, pages 1133-1138).

The claims are broadly drawn towards a method for conveying resistance to BNYVV to a sugar beet plant, comprising preparing a DNA fragment of at least 15 nucleotides in a sequence that is at least 70%, 80%, 90%, or 95% homologous to the corresponding nucleotide sequence of the genomic RNA 1 of the BNYVV, introducing the DNA fragment into a sugar beet plant cell, and regenerating a transgenic sugar beet plant from the transformed cell; a transformation vector harboring said fragment; a plant cell exhibiting a resistance to BNYVV, comprising said fragment; a method for the production of a sugar beet plant resistant to BNYVV comprising regenerating said plant cell; a sugar beet plant comprising said cells.

Baulcombe discusses the successful expression of viral replicase genes and portions of viral replicase genes in transgenic plants to confer viral resistance to those plants. In some examples, the resistance was conferred through RNA-mediated homology-dependent resistance, and in other examples the resistance was protein-based (pages 1839-1840).

Baulcombe does not teach RNA1 of BNYVV and transgenic sugar beet.

Saito et al. compare the nucleotide sequences of the "F2" and "S" isolates of BNYVV, including the sequence of RNA 1, which consists of 6746 nucleotides, that encodes the viral

replicase, cite functional domains of the replicase. Saito et al. also assert that BNYVV is responsible for rhizomania disease of sugar beet (pages 2165-2171).

Hall et al. teach genetic transformation of sugar beet cells and regeneration of the transgenic cells to transgenic plants (pages 1133-1137).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to use the methods of replicase-mediated viral resistance discussed by Baulcombe with the BNYVV replicase-encoding sequences taught by Saito et al. It would have been obvious to insert the BNYVV replicase-encoding nucleotide sequences taught by Saito et al., operably linked to transcription and translation regulatory sequences, into a plant transformation vector and transform the vector into a plant, to confer BNYVV resistance to that plant. It also would have been obvious to express fragments of the replicase-encoding nucleotide sequences, which resides on genomic RNA 1, as Baulcombe also discusses viral resistance conferred by the expression of fragments of replicase-encoding nucleotide sequences, and viral resistance conferred by gene silencing. As it was known that in the gene silencing mechanism, genes that share high sequence homology are co-suppressed, the choice of fragment of RNA 1 that one would have expressed, including nucleotides, 153-3258, 169-539, 1226-1638, and 2754-3192, amounted to an optimization of process parameters. One would have been motivated to express nucleotide sequences from the BNYVV replicase to confer resistance to it in plants, as the discussion in Baulcombe demonstrates that such a strategy had been successfully used to confer resistance against numerous viruses. It would have been obvious to transform the RNA 1 sequences into any plant that is a host to BNYVV. One would have been motivated to introduce and express the sequences in sugar beet plants, using the transformation method taught by Hall et

al., as it was well known, and asserted by Saito et al., that BNYVV causes rhizomania disease in sugar beet.

8. Claims 30-61 are rejected.

Contact Information

Any inquiry concerning this communication from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist, whose telephone number is 703-308-0196.

March 28, 2003

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER